Synthesis and Reactions of 2-[1-Methyl-1-(pyrrolidin-2-yl)ethyl]-1*H*-pyrrole and Some Derivatives with Aldehydes: Chiral Structures Combining a Secondary-Amine Group with an 1*H*-Pyrrole Moiety as Excellent H-Bond Donor

by **Anca Pordea**[a])[1]), **Helen Stoeckli-Evans**[b]), **Claudio Dalvit**[c]), **Reinhard Neier***[a])

[a]) Institut de chimie, Université de Neuchâtel, Avenue Bellevaux 51, CH-2000 Neuchâtel (phone: +41(0)32 718 2428; fax +41(0)32 718 2511; e-mail: Reinhard.Neier@unine.ch)
[b]) Institut de physique, Université de Neuchâtel, Avenue Bellevaux 51, CH-2000 Neuchâtel (phone: +41(0)32 718 2426; e-mail: Helen.Stoeckli-Evans@unine.ch)
[c]) Service analytique facultaire, Université de Neuchâtel, Avenue Bellevaux 51, CH-2000 Neuchâtel (phone: +41(0)32 718 2435; e-mail: Claudio.Dalvit@unine.ch)

Dedicated to Professor *Dieter Seebach* on the occasion of his 75th birthday for his remarkable contributions to chemistry

The synthesis of compound **2** and its derivatives **6** and **8** combining a pyrrolidine ring with an 1*H*-pyrrole unit is described (*Scheme 2*). Their attempted usability as organocatalysts was not successful. Reacting these simple pyrrolidine derivatives with cinnamaldehyde led to the tricyclic products **3b**, **9b**, and **10b** first (*Scheme 1*, *Fig. 2*). The final, major products were the pyrrolo-indolizidine tricycles **3a**, **9a**, and **10a** obtained *via* the iminium ion reacting intramolecularly with the nucleophilic β-position of the 1*H*-pyrrole moiety (*cf. Scheme 1*).

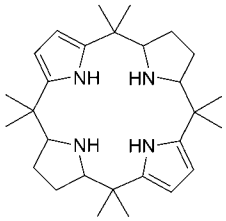
1. Introduction. – The re-discovery of the *Hajos–Parrish–Eder–Sauer–Wiechert* reaction [1] led to the realization that proline is a privileged skeleton for the synthesis of chiral organocatalysts [2], capable of combining high selectivities with broad applicability [3]. Proline, historically the first successful organocatalyst, displays a simple design combining the pyrrolidine ring carrying a chiral center with an acidic or at least strongly H-bond donating substituent. After the initial reports of the efficient use of proline as chiral catalyst by two industrial laboratories [4], substantial efforts were made to modify the structure of proline with the goal to obtain more selective catalysts and to deepen our knowledge [5]. Combining an oversimplified, certainly incomplete, mechanistic picture [3a][3e][6] with the ease with which the proline structure can be tuned [6d][7] and then tested by a screening approach [8] has led to an 'explosive growth in this area since the year 2000' [6b][7b]. An essential part of the operationally useful mechanistic picture is the inclusion of H-bonds as an important factor for obtaining good enantioselectivities [3e][6a][6n][6o].

[1]) New address since 1 August, 2012: Department of Chemical & Environmental Engineering, University of Nottingham, University Park, Nottingham NG7 2RD, UK (phone: +44(0)115 951 4640; e-mail: Anca.Pordea@nottingham.ac.uk)

H-Bonding interactions play a key role in various enzymatic mechanisms, by participating both in electrophile activation and in substrate recognition [9]. Chemists have also discovered that small organic H-bond-donor motifs can catalyze organic transformations, in association or not with other functional groups [2b][10]. Urea and thiourea derivatives have been successfully used as catalysts for the activation of imine or carbonyl functionalities, *via* bidentate H-bonding interaction [2b][7e][7f][7h][10a–10d][11]. Proline acts as a multifunctional catalyst: the secondary-amine moiety activates the carbonyl group through nucleophilic enamine formation, while the H-donating carboxylic acid group orients and activates the electrophile [6a][6n][6o][10b]. The understanding of the simplified, empirically useful mechanism of proline-catalyzed reactions was the starting point for the development of novel organocatalysts bearing H-donor moieties. In addition, since the publications of *Barbas*, *List*, *MacMillan*, and their co-workers on enantioselective organocatalysis based on iminium and enamine formation [1a][1c], the pyrrolidine motif has been widely used as a carbonyl activating organocatalyst, *via* iminium or enamine formation [3e][12]. Structures containing a pyrrolidine moiety in conjunction with moieties involved in H-bonding, such as 1*H*-imidazole, 1*H*-tetrazoles [13], pyridineamines, *etc.*, have been proposed [14]. However, 1*H*-pyrrole–pyrrolidine structures have not yet been envisaged.

Prompted by the results described in [15] and given the interesting H-bonding properties observed with these structures [16], we decided to study the synthesis and properties of simple pyrrolidine derivatives containing an 1*H*-pyrrole ring as potential H-bond donor. The 1*H*-pyrrole has been included in the design of chiral catalysts by the *Jacobsen* group fulfilling a structural role exclusively [10d][17]. To the best of our knowledge, 1*H*-pyrroles have not been reported to be used as H-bond donors in the design of organocatalysts.

During a project directed towards the understanding of N-containing macrocycles, our group became interested in studying the hydrogenation of calix[4]pyrroles [15a][15b]. The purpose of these efforts was to obtain fully saturated N-macrocycles with a rigid skeleton and to test the properties of their metal complexes [18]. The nontrivial hydrogenation of calix[4]pyrrole initiated a long lasting study of different hydrogenation conditions and catalysts to optimize the formation and isolation of the fully reduced calix[4]pyrrolidine. During the hydrogenation process, we observed the formation of partially reduced macrocycles **1** containing alternating 1*H*-pyrrole–pyrrolidine structures, which to our surprise could not be further hydrogenated to the completely saturated structure [15c]. Upon examination of the reactivity and of the



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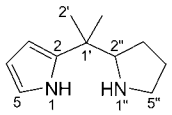


2

X-Ray structure of the major stereoisomer of **1**, we concluded that this partially reduced macrocycle was characterized by an extraordinary tight intramolecular H-bonding network, connecting the 1*H*-pyrrole N–H with the lone pair of the neighboring pyrrolidine N-atom [15b]. We hypothesized that this network might be responsible for the unusually low reactivity of the pyrrolidine unit, observed in preliminary studies [19].

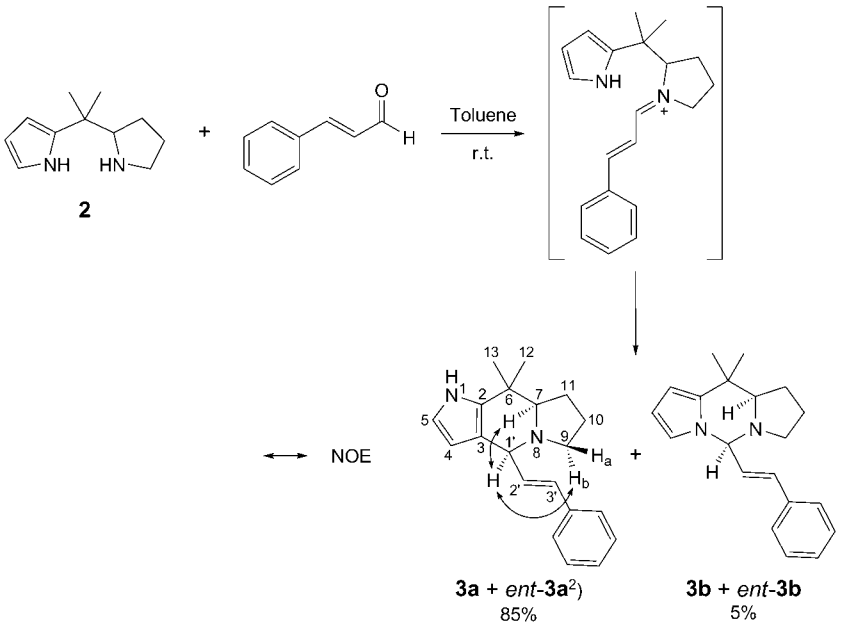
2. Results and Discussion. – *Reaction of* **2** *with* (E)*-Cinnamaldehyde.* The starting point of this study is compound **2**, which can be easily obtained by condensation of two 1*H*-pyrrole rings with one molecule of acetone, followed by heterogeneous hydrogenation on Pd/C [16b]. In contrast to the calix[2]pyrrole[2]pyrrolidine macrocycle **1**, this structure only contains one stereogenic center and can be more easily modified at the 1*H*-pyrrole ring, thus giving access to a family of molecules with modulated properties. We intended to test the potential of the unmodified compound **2** to function as organocatalyst in a series of well studied transformations, which have been demonstrated to be successfully catalyzed by proline. We also planned to modify **2** in the α-position of the 1*H*-pyrrole moiety thereby modifying the electronic properties of the 1*H*-pyrrole ring.

We tested **1** first. As expected, **1** did not show any reactivity towards iminium formation under the conditions tested by us. This is certainly due to the low reactivity of the pyrrolidine moiety buried inside the macrocycle and 'protected' by the H-bond network [15c]. This result is in accordance with the partial or even total protection of the pyrrolidine rings in the macrocycle **1** against many acylation conditions [15c][19].

When we tested compound **2** as organocatalyst for the *Michael* addition of nitromethane or dimethyl malonate to (*E*)-cinnamaldehyde (=(2*E*)-3-phenylprop-2-enal), preliminary results showed no trace of product formation [20]. The *Diels–Alder* reaction between (*E*)-cinnamaldehyde and cyclopentadiene in the presence of **2** was also unsuccessful. Therefore, we concentrated our efforts on studying the reactivity of the 1*H*-pyrrole–pyrrolidine system towards iminium formation. We chose (*E*)-cinnamaldehyde as reagent for the condensation reaction, so as to minimize the risk of aldol condensation during our studies. To our surprise, we observed the formation of one major product, which was identified by NMR spectroscopy as the pyrroloindolizidine tricycle **3a**, when mixing **2** and (*E*)-cinnamaldehyde in stoichiometric amounts in anhydrous toluene at room temperature (*Scheme 1*). Molecular sieves were used to remove H_2O formed during the reaction and to ensure complete transformation. Upon careful investigation of the literature, we found one report of a similar intramolecular cyclization reaction, starting from a 1*H*-pyrrole–oxazolidinone system [21]. The reactivity of 1*H*-pyrrole towards iminium ions or enamines is known; however, reactions taking place at the α-position of the 1*H*-pyrrole seem to be generally preferred according to the published results [20][22]. Similarly to the results published by *Sisti* and co-workers [21], also our cyclization reaction was diastereoselective, with the protons H–C(7) and H–C(1′) being *cis*[2]). The 2D-ROESY technique was used to determine the relative configuration of compound **3a**. We suggest that the diastereoselectivity of the reaction is probably due to the conformationally preferred

[2]) Arbitrary atom numbering; for systematic names, see *Exper. Part.*

Scheme 1. *Reaction between* **2** *and* (E)*-Cinnamaldehyde, Leading to the Formation of the Cyclized Products* **3a** *and* **3b**



equatorial arrangement of both the 1-methyl-1-(1*H*-pyrrol-2-yl)ethyl and the phenylethenyl moiety.

It is likely that **3a** is obtained by intramolecular electrophilic substitution by the iminium ion intermediate at the electron-rich 1*H*-pyrrole system. The product can be tentatively interpreted as a hint for the occurrence of the iminium ion followed by the reaction with the electron rich heterocycle. Unfortunately the intramolecular reaction with the electrophilic 1*H*-pyrrole ring seems to be faster than the intended intermolecular transformations needed for the organocatalytic cycle.

Following the course of the reaction in deuterated benzene at room temperature in the NMR tube, no ^{1}H-NMR signal corresponding to the iminium ion could be observed (expected at δ(H) *ca.* 8 ppm), thus suggesting that the cyclization reaction is too fast to be observed by NMR under these conditions. On the other hand, the time-dependent NMR experiment showed the formation of a second cyclization product, which we identified as the regioisomer **3b** in which the substitution is located at the N-atom of the 1*H*-pyrrole (*Fig. 1*). The reaction reached equilibrium after 3.5 h. After this time, the conversion reached 96%, with formation of compound **3a** in 85% yield and of its regioisomer **3b** in 6% yield, and of an additional, not yet completely identified minor compound in 5% yield (see *Supporting Information*[3])). In our hands, separation of the three reaction products by column chromatography (neutral alumina) proved to be very difficult, and we characterized the mixture by 1D and 2D ^{1}H-NMR spectroscopy.

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[3]) *Supporting Information* is available from the corresponding author.

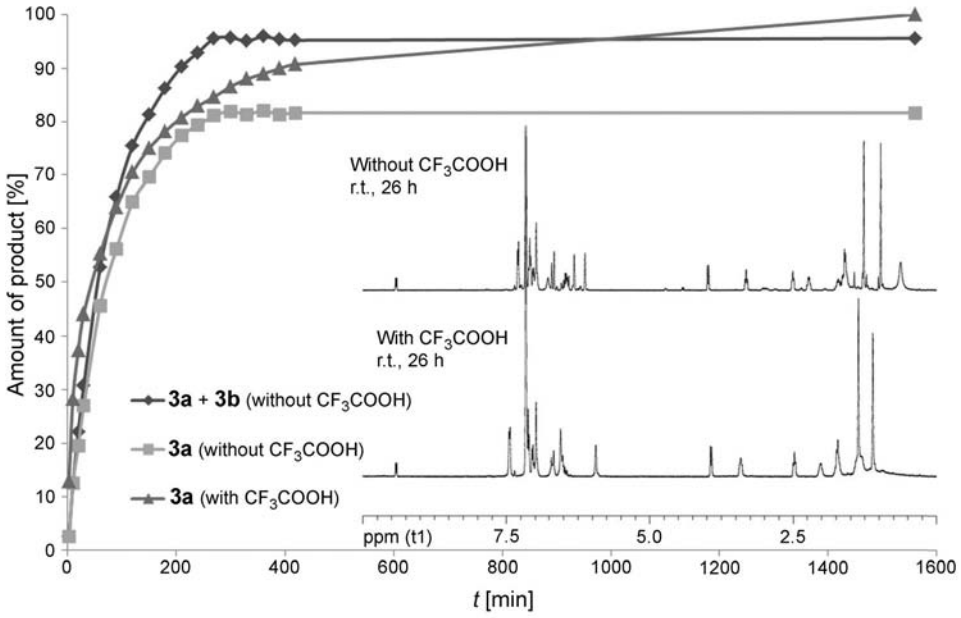


Fig. 1. *Comparison of the reactions between* **2** *and (*E*)-cinnamaldehyde, in the presence and in the absence of CF_3COOH.* The reaction time course was followed by ^{1}H-NMR in C_6D_6 at r.t.

GC/MS Analysis of the mixture showed the presence of two products with identical molecular mass and nearly the same retention time, corresponding to isomers **3a** and **3b**, as well as of the additional by-product with a different retention time.

In the published report by *Sisti* and co-workers, trifluoroacetic acid (CF_3COOH) was shown to promote intramolecular cyclization between an oxazolidinone and a *N*-methyl substituted 1*H*-pyrrole [21]. In our case, addition of 1 equiv. of CF_3COOH slightly increased the initial reaction rate and allowed the reaction to reach completion. The rate of the reaction became slower after the first 1.5 h. Most importantly, the reaction in the presence of CF_3COOH proved to be completely regioselective. Only the presence of the pyrroloindolizine **3a** arising from cyclization at the β-position of the 1*H*-pyrrole could be observed during the reaction (*Fig. 1*).

Acceleration of the condensation reaction in the presence of CF_3COOH could be explained by acid-promoted iminium formation. In our case, the 1*H*-pyrrole NH of **2** could be responsible for this activation, which could explain the relatively small influence of CF_3COOH on the reaction. When (*E*)-cinnamaldehyde was treated with pyrrolidine in C_6D_6 at room temperature, in the absence of CF_3COOH, no iminium signal was detected by NMR, and the reaction proceeded to an equilibrium, with formation of the hemiaminal intermediate in a 1:1 ratio with the starting material. Addition of 1 equiv. of 1*H*-pyrrole had no influence on this equilibrium. Normally it is assumed that iminium formation between the pyrrolidine ring and (*E*)-cinnamaldehyde should occur under acid catalysis. Since the reaction between (*E*)-cinnamaldehyde and the 1*H*-pyrrole–pyrrolidine compound **2** proceeds smoothly, it is likely that

the NH of the 1*H*-pyrrole moiety provides the acidic protons necessary to for iminium formation.

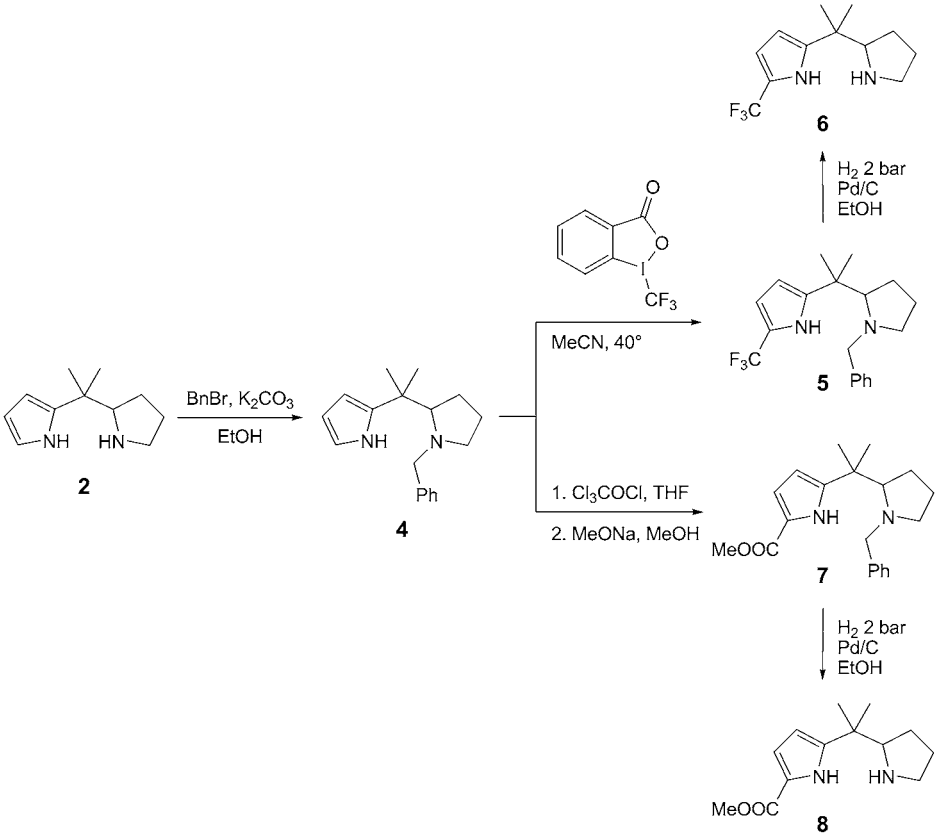
*Synthesis and Reactivity of the Deactivated 1*H-*Pyrrole Compounds* **6** *and* **8**. To reduce the nucleophilicity of the 1*H*-pyrrole ring, we synthesized substituted 1*H*-pyrrole–pyrrolidine structures bearing electron-attracting substituents at position 5 on the 1*H*-pyrrole ring and tested their reactivity in the reaction with (*E*)-cinnamaldehyde. During our studies, we became aware of the work of *Thompson* and co-workers [23], who tested different conditions for the synthesis of substituted dimethyldipyrromethane (=2,2′-(1-methylethylidene)bis[1*H*-pyrrole] derivatives; an unusual cyclization reaction took place during the condensation of 1*H*-pyrrole rings with methyl ketone electrophiles, during which the N-atom of the 1*H*-pyrrole underwent alkylation with an electrophilic intermediate. In this study it was reported that 1*H*-pyrroles deactivated by conjugation with an electron withdrawing ester group did not undergo such an unusual cyclization [23]. Therefore, we proceeded to α-substitution at the 1*H*-pyrrole moiety of **2** with electron-withdrawing groups, with the purpose of slowing down the cyclization process and of promoting nucleophilic attack of the iminium intermediate by other nucleophiles present in the system, thereby hopefully creating compounds suitable for organocatalysis. Moreover, we hypothesized that an electron-withdrawing group might enhance the acidity of the 1*H*-pyrrole NH, and therefore its H-bonding capacity [24].

We first proceeded to the introduction of a trifluoromethyl substitution at the α-position of the 1*H*-pyrrole moiety of **2** by a method developed by *Togni* and co-workers (*Scheme 2*) [25]. Pyrrolidine protection ($\rightarrow$**4**) and deprotection steps were necessary, and the benzyl group was chosen for this purpose, due to the ease of removal at the end of the reaction (**5** $\rightarrow$ **6**). The corresponding trifluoromethyl-substituted 'dimethylpyrropyrrolidinylmethane' (=2-[1-methyl-1-(pyrrolidin-2-yl)ethyl]-1*H*-pyrrol) **6** could be analyzed by X-Ray diffraction, showing tight packing due to H-bonding between the 1*H*-pyrrole and the pyrrolidine units, as already reported for **2** (see *Exper. Part*) [16b].

Treatment of the CF_3-substituted 1*H*-pyrrole **6** with (*E*)-cinnamaldehyde in toluene afforded the cyclized regio- and diastereoiosomer **9a** almost exclusively. Following the reaction course by ^{1}H-NMR in C_6D_6 at room temperature showed first the formation of the *N*-cyclized regioisomer **9b**, which then equilibrated to the *C*-cyclized regioisomer **9a** (*Fig. 2*). This suggests that the *N*-cyclization is under kinetic control, while the *C*-cyclized product is thermodynamically favored. The starting material **6** was completely consumed at the end of the reaction, while **9a** was obtained in 95% yield, as determined by ^{1}H-NMR. A third product, which could not be completely identified by ^{1}H-NMR, was formed in 5% yield, while no trace of the *N*-cyclized **9b** could be observed at the end of the reaction. Addition of CF_3COOH disfavored the *N*-cyclized product, which formed in a smaller amount and disappeared faster than in the absence of CF_3COOH. Moreover, the reaction proceeded slower in the presence of CF_3COOH.

Introduction of the electron withdrawing CF_3 substituent at the α-position of the 1*H*-pyrrole ($\rightarrow$**6**) showed no significant effect on the total reaction rate. However, the regioselectivity of the reaction was enhanced in the presence of the CF_3-substituent, and the reaction proceeded to complete consumption of the starting material as compared to the unsubstituted **2**.

Scheme 2. *Synthesis of Compounds* **6** *and* **8**



We then tested the effect of a carboxylate ester substitution at the α-position of the 1*H*-pyrrole moiety of **2**, which deactivates the 1*H*-pyrrole by conjugation and introduces at the same time a supplementary H-bond acceptor [26]. Compound **7** was prepared by a known procedure, involving introduction of a trichloroacetyl substituent, followed by substitution of the CCl_3 group by MeO (*Scheme 2*) [27]. Removal of the benzyl protecting group afforded compound **8**. When **8** was treated with (*E*)-cinnamaldehyde in C_6D_6 at room temperature, the reaction proceeded much slower than in the case of **2** and **6**, with initial formation of the *N*-cyclized regioisomer **10b** in up to 46% yield in the first 5 h, followed by its decrease over the next 56 h and its equilibration into the *C*-cyclized regioisomer **10a**. After 56 h we stopped following the reaction. The transformation was not complete, and the equilibrium was not reached: only 74% of the starting material **8** was transformed. The reaction was less diastereoselective in this case, and the *C*-cyclized diastereoisomer **10c** was formed in 20% yield only. Addition of 1 equiv. CF_3COOH greatly decreased the reaction rate of the formation of all three compounds **10a**–**10c** (*Fig. 3*). This result was encouraging, because it established that the cyclization preference could be reversed, due to

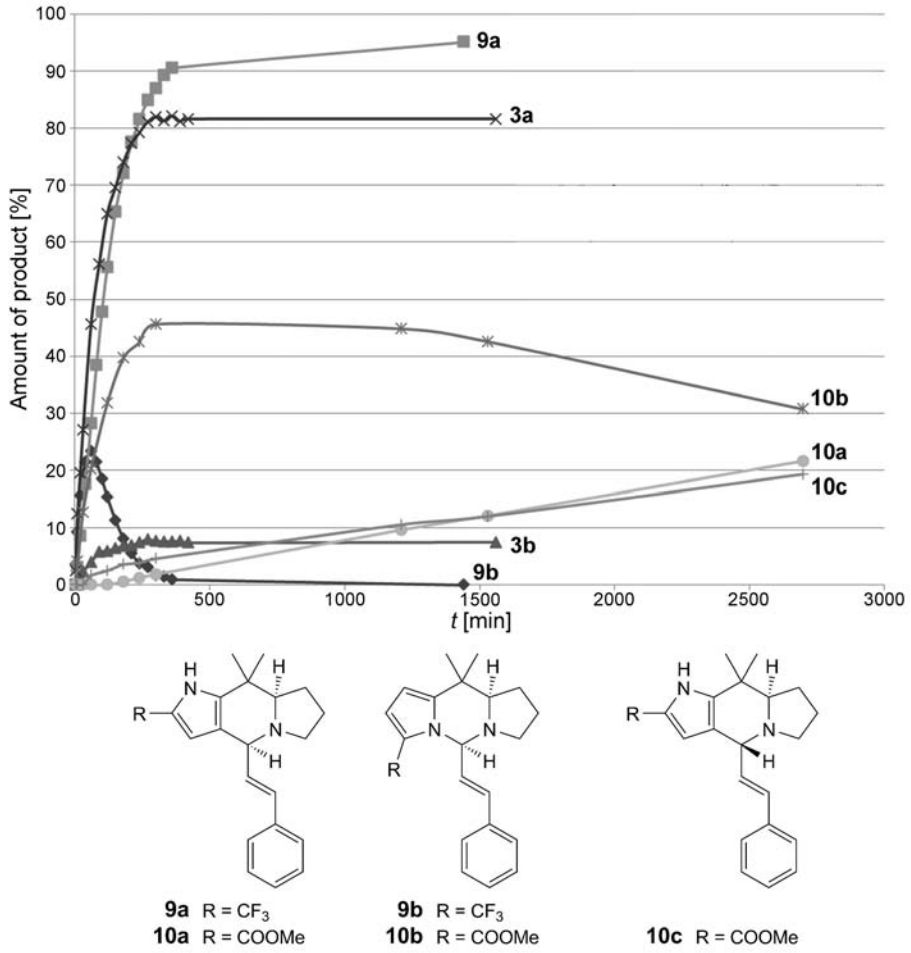


Fig. 2. *Time course for the formation of compounds* **3a** *and* **3b**, **9a** *and* **9b**, *and* **10a**, **10b**, *and* **10c** *followed by* ^{1}*H-NMR*

deactivating substitutions at position 5 of the 1*H*-pyrrole ring of **2**. However, an attempt to use compound **8** as organocatalyst in the reaction between (*E*)-cinnamaldehyde and dimethyl malonate or nitromethane did not afford the desired *Michael* addition product neither.

3. Conclusions. – The present study describes an easy access to three compounds of a novel structural type combining a basic pyrrolidine ring with 1*H*-pyrrole as good H-bond donor linked by a quaternary C-center. Our ^{1}H-NMR studies showed that these compounds **2**, **6**, and **8** react with (*E*)-cinnamaldehyde in an intramolecular fashion. The reaction products **3b**, **9b** and **10b** formed first retained the oxidation state of the aldehyde C-atom and, therefore, resemble the oxazolidinones isolated from the

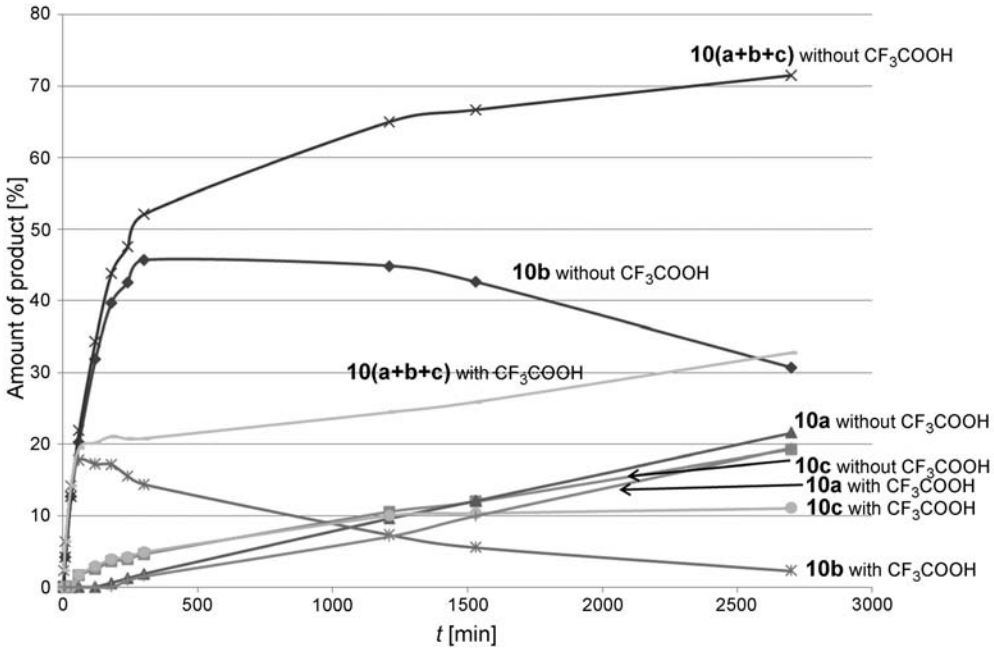


Fig. 3. *Time course for the formation of compounds* **10a**–**10c** *in the absence and in the presence of* CF_3COOH

reaction between the doubly silylated proline and pivaldehyde [6e]. Depending on the substituent at the 5 position of the 1*H*-pyrrole, these products were then irreversibly transformed into the thermodynamically more stable products **3a**, **9a**, and **10a** by an intramolecular *Mannich*-type reaction with the electrophilic 3 position of their 1*H*-pyrrole moiety. This intramolecular reaction of the iminium C-atom from cinnamaldehyde with the electrophilic C(3)-atom of the 1*H*-pyrrole moiety corresponds to one of the reaction types observed intermolecularly in organocatalytic transformations. The formation of the products **3a**, **9a**, and **10a** was diastereoselective and thermodynamically controlled. The structure of the minor products **3c**, **9c** and **10c** was attributed tentatively to the other diastereoisomer. The presence of the strong acid CF_3COOH accelerated the transformation of compound **2**, whereas the transformation of **6** and **8** was slowed down by CF_3COOH.

The diversity of reaction pathways opened up by the activation of C=O compounds by secondary-amine moieties such as typically in proline or imidazolidinone derivatives is overwhelming. The mechanistic intricacies are slowly deciphered and show a much more complex picture than the mechanistic rules of thumb, which have been used successfully to optimize the screening process used for the development of many of the reactions published in the literature. The success of organocatalysis is a testimony to the utility of simplified mechanistic proposals and to the efficiency of effective analytical screening methods. For our new structures **2**, **6**, and **8**, we identified the reactivity needed for a catalytic process; a parasitic intramolecular reaction between the iminium

ion formed from cinnamaldehyde and these pyrrolidine compounds blocked catalytic conversions. Modification of the electronic properties of the 1*H*-pyrrole moiety influenced the path of the reaction in a way predicted by the electronic properties of the substituents. We did not yet discover reaction conditions or substituent patterns allowing the use of our type of molecules in organocatalysis, despite the fact that the inherent reactivity needed for a catalytic cycle was demonstrated.

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Experimental Part

General. All the reagents were purchased from commercial sources and used as such, unless specified in the literature describing their syntheses. Solvents for extraction and chromatography were of anal. grade. Column chromatography (CC): 63–200 mesh SiO_2 (*Brunschwig*). Anal. TLC: SiO_2 plates with *QF-254* indicator (*Merck*); detection by UV light (254 nm) and/or after treatment with phosphomolybdic acid. M.p.: *Gallenkamp* apparatus; uncorrected. IR Spectra: *Fourier*-transform spectrophotometer *Perkin Elmer Spectrum One*, version *B*; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *DPX-400-Bruker* spectrometer at r.t. for 1D plots and *Avance-400-Bruker* spectrometer at 23° with typically a mixing time of 300 or 400 ms for ROESY; δ in ppm rel. to $SiMe_4$, J in Hz. ESI-MS: *Finnigan-LCQ* mass spectrometer; in *m*/*z* (rel %). Anal. GC-MS: *Polaris-Q-Trace* GC instrument (*Finnigan*) fitted with a flame-ionization detector (H_2 carrier gas, 1 ml min^{-1}, detector temp. 300°) and a *ZB-5MS* column (30 m × 0.25 mm × 0.25 μm), and MS acquired in EI mode (70 eV); in *m*/*z* (rel %).

*2-[1-Methyl-1-(pyrrolidin-2-yl)ethyl)-1*H*-pyrrole* (**2**) [16b]. In an autoclave vessel were introduced 2,2′-(1-methylethylidene)bis[1*H*-pyrrole] [16a] (2 g, 11.5 mmol, 1 equiv.), 10% Pd/C (524 mg, 0.043 equiv. Pd), and MeOH/AcOH 4 : 1 (*v*/*v*; 100 ml). The suspension was stirred for 20 h at r.t. under 65 bar H_2. Then the Pd/C was filtered on *Celite*, the *Celite* pad washed with CH_2Cl_2 (3×), and the combined filtrate concentrated to give a yellow slurry to which 2M NaOH (175 ml) and CH_2Cl_2 (100 ml) were added. The aq. phase was extracted with CH_2Cl_2 (3×), the combined org. phase dried (K_2CO_3) and concentrated, and the resulting residue purified by CC(SiO_2; AcOEt/MeOH/Et_3N 95 : 5 : 1: 1.665 g (81%) of **2**. Colorless crystals. M.p. 75°. IR (KBr): 3413*w*, 3150.4*m*, 3081.5*m*, 2966.4*s*, 2872.3*s*, 1618.4*w*, 1566.8*m*, 1452.5*w*, 1423.4*s*, 1070.2*s*, 946.2*s*, 880.1*m*, 725.7*s*, 714.4*s*. ^1H-NMR ($CDCl_3$): 10.3 (br. *s*, H–N(1)); 6.69–6.66 (*m*, H–C(5)); 6.14–6.09 (*m*, H–C(4)); 5.96–5.92 (*m*, H–C(3)); 3.11 (*t*, J = 8.1, H–C(2″)); 2.91–2.88 (*m*, CH_2(5″)); 2.04 (br. *s*, H–N(1″)); 1.78–1.72 (*m*, CH_2(3″)); 1.66–1.56 (*m*, CH_2(4″)); 1.33 (*s*, Me); 1.25 (*s*, Me); 1.23–1.17 (*m*, 1 H, CH_2)3″)). ^{13}C-NMR ($CDCl_3$): 139.4 (C(2)); 116.0 (C(5)); 106.4 (C(4)); 103.8 (C(3)); 68.9 (C(2″)); 46.7 (C(5″)); 37.2 (Me_2C(1′)); 29.4 (Me); 26.9 (C(3″)); 25.8 (C(4″)); 24.8 (Me). ESI-MS: 217.2 (30, $[M+K]^+$), 207.2 (20), 201.2 (50, $[M+Na]^+$), 179.2 (100, $[M+H]^+$). HR-ESI-MS: 179.1544 ($C_{11}H_{18}N_2^+$, $[M+H]^+$; calc. 178.1470).

*2-{1-Methyl-1-[1-(phenylmethyl)pyrrolidin-2-yl]ethyl}-1*H*-pyrrole* (**4**). To a soln. of **2** (3.175 g, 17.8 mmol, 1 equiv.) in EtOH (42 ml) was added K_2CO_3 (5.17 g, 35.6 mmol, 2.1 equiv.) and benzyl bromide (2.12 ml, 17.8 mmol, 1 equiv.), and the soln. was stirred overnight. The EtOH was evaporated, and AcOEt and H_2O were added. The aq. phase was extracted twice with AcOEt (2×), the combined org. phase dried (Na_2SO_4) and concentrated, and the crude product purified by CC(SiO_2, cyclohexane/AcOEt 95 : 5): **4** (4.04 g, 85%). Yellow oil. IR (KBr): 3397.6*s* (br.), 3061.9*w*, 3027.8*w*, 2964.8*s*, 2868.2*s*, 2799.5*m*, 1556.9*m*, 1494.8*w*, 1452.7*m*, 1381.7*w*, 1334.2*w*, 1107.9*m*, 1070.2*m*, 1030.5*m*, 785.6*m*, 718.9*s*, 699.2*s*. ^1H-NMR ($CDCl_3$): 9.76 (br. *s*, H–N(1)); 7.48–7.41 (*m*, 4 H, Ph); 7.37–7.35 (*m*, 1 H, Ph); 6.73–6.72 (*m*, H–C(5)); 6.16–6.15 (*m*, H–C(4)); 6.00–5.98 (*m*, H–C(3)); 4.17 (*d*, J = 13.1, 1 H, PhCH_2); 3.54 (*d*, J = 13.1, 1 H, PhCH_2); 2.86 (*dd*, J = 8.85, 5.5, H–C(2″)); 2.79–2.73 (*m*, 1 H, CH_2(5″)); 2.47–2.41 (*m*, 1 H, CH_2(5″)); 1.97–1.88 (*m*, 1 H, CH_2(3″)); 1.62–1.53 (*m*, 1 H, CH_2(4″)); 1.52–1.45 (*m*, 1 H, CH_2(3″)); 1.55 (*s*, Me); 1.34 (*s*, Me); 1.16–1.08 (*m*, 1 H, CH_2(4″)). ^{13}C-NMR ($CDCl_3$): 140.7 (C_{ipso}); 138.9

(C(2)); 128.5 (CH(Ph)); 128.45 (CH(Ph)); 127.0 (CH)Ph)); 116.5 (C(5)); 106.8 (C(4)); 104.2 (C(3)); 74.8 (C(2″)); 63.6 (Ph*C*H$_2$); 54.9 (C(5″)); 39.0 (Me$_2$*C*(1′)); 29.7 (Me); 28.9 (C(3″)); 25.2 (Me); 24.2 (C(4″)). EI-MS: 269.13 (10, $[M+H]^+$), 267.12 (10, $[M-H]^+$), 160.1 (25, $[M-C_4H_3NHC(Me)_2]^+$), 91.12 (100, $PhCH_2^+$). HR-ESI-MS: 269.2013 ($C_{18}H_{25}N_2^+$, $[M+H]^+$; calc. 269.2012).

*2-[1-Methyl-1-[(phenylmethyl)pyrrolidin-2-yl]ethyl]-5-(trifluoromethyl)-1*H*-pyrrole* (**5**). According to [25]: A suspension of **4** (413 mg, 1.54 mmol, 1 equiv.) and 1-(trifluoromethyl)-1,2-benziodoxol-3(1*H*)-one (730 mg, 2.3 mmol, 1.5 equiv.) in anh. MeCN (5 ml) was stirred under N_2 at 40° for 18 h. The brown-red soln. was concentrated and CH_2Cl_2 (20 ml) added. The org. phase was washed successively with sat. $NaHCO_3$ and NaCl solns. (20 ml of each), dried (Na_2SO_4), and concentrated and the resulting crude product purified by CC(SiO_2, cyclohexane/AcOEt 98:2): **5** (290 mg, 56%). Yellow oil. IR (KBr): 3294.1*s* (br.), 3025.2*m*, 2969.9*s*, 2868.3*m*, 2806.7*w*, 1608.4*w*, 1577.6*w*, 1504.8*s*, 1451.7*m*, 1321.7*s*, 1236.7*m*, 1149.7*s*, 1102.5*s*, 1037.8*w*, 943.6*m*, 783.1*s*, 732.9*m*, 699.8*m*. ^{1}H-NMR ($CDCl_3$): 10.9 (br. *s*, H–N(1)); 7.41–7.38 (*m*, 4 H, Ph); 7.33–7.30 (*m*, 1 H, Ph); 6.45 (*s*, H–C(4)); 5.95 (*s*, H–C(3)); 4.24 (*d*, *J* = 13, 1 H, PhC*H*$_2$); 3.58 (*d*, *J* = 13, 1 H, PhC*H*$_2$); 2.86 (*dd*, *J* = 8.6, 6.2, H–C(2″)); 2.74 (*dt*, *J* = 10.5, 6.1, 1 H, CH_2(5″)); 2.45 (*dt*, *J* = 10.5, 6.7, 1 H, CH_2(5″)); 1.97–1.88 (*m*, 1 H, CH_2(3″)); 1.61–1.51 (*m*, 1 H, CH_2(4″)); 1.49 (*s*, Me); 1.40–1.32 (*m*, 1 H, CH_2(4″)); 1.29 (*s*, Me); 1.17–1.07 (*m*, 1 H, CH_2(3″)). ^{13}C-NMR ($CDCl_3$): 142.2 (C(2)); 140.2 (C_{ipso}); 128.6 (CH(Ph)); 127.9 (CH(Ph)); 127.1 (CH(Ph)); 121.7 (*q*, *J* = 266, CF_3); 118.9 (*q*, *J* = 39, C(5)); 108.5 (*q*, *J* = 2.9, C(4)); 105.2 (C(3)); 74.8 (C(2″)); 63.4 (Ph*C*H$_2$); 54.8 (C(5″)); 38.8 (Me$_2$*C*(1′)); 30.4 (Me); 29.0 (C(3″)); 24.9 (Me); 24.1 (C(4″)). EI-MS: 337.18 (12, $[M+H]^+$), 250.22 (12), 160.1 (100, $[M-CF_3C_4H_2NHC(Me)_2]^+$), 91.6 (29, $PhCH_2^+$). HR-ESI-MS: 337.1882 ($C_{19}H_{24}F_3N_2^+$, $[M+H]^+$; calc. 337.1886).

*2-[1-Methyl-1-(pyrrolidin-2-yl)ethyl]-5(trifluoromethyl)-1*H*-pyrrole* (**6**). To a soln. of **5** (851 mg, 2.53 mmol, 1 equiv.) in EtOH (50 ml) was added 10% Pd/C (134 mg, 0.05 equiv. Pd), and the suspension was shaken under 2 bar H_2 at r.t. overnight. The mixture was then filtered on *Celite*, the *Celite* pad thoroughly washed with EtOH, the solvent evaporated, and the crude product purified by CC (basic alumina, 0.5% MeOH/CH_2Cl_2): 192 mg (31%) of **6**. Colorless-yellowish crystals. M.p. 50°. IR (KBr): 3280*w*, 3137.4*w*, 3100*m*, 2967.6*s*, 2877.4*s*, 1700.1*w*, 1595.2*w*, 1501.1*s*, 1366.3*m*, 1349.3*s*, 1254*m*, 1174.9*m*, 1155.9*s*, 1112.6*s*, 945.5*s*, 853.3*m*, 768.2*m*. ^{1}H-NMR ($CDCl_3$): 11.2 (br. *s*, H–N(1)); 6.40 (*s*, H–C(4)); 5.9 (*s*, H–C(3)); 3.13 (*t*, *J* = 8.0, H–C(2″)); 2.94–2.88 (*m*, CH_2(5″)); 2.1 (br. *s*, H–N(1″)); 1.85–1.71 (*m*, 1 H, CH_2(3″)); 1.71–1.47 (*m*, CH_2(4″)); 1.32 (*s*, Me); 1.23 (*s*, Me); 1.17–1.03 (*m*, 1 H, CH_2(3″)). ^{13}C-NMR ($CDCl_3$): 142.8 (C(2)); 121.7 (*q*, *J* = 266, CF_3); 118.4 (*q*, *J* = 39, C(5)); 108.3 (*q*, *J* = 2.9, C(4)); 104.9 (C(3)); 68.6 (C(2″)); 46.5 (C(5″)); 37.2 (Me$_2$*C*(1′)); 29.7 (Me); 27.0 (C(3″)); 25.8 (C(4″)); 24.6 (Me). ESI-MS: 247.1 (100, $[M+H]^+$), 227.2 (10, $[M-F]^+$). HR-ESI-MS: 247.1414 ($C_{12}H_{17}F_3N_2^+$, $[M+H]^+$; calc. 246.1344).

Crystal Structure Analysis of **6**[4]) (*Figs. 4* and *5*). Suitable crystals of **6** were obtained as colorless rods by slow evaporation of a soln. of **6** in pentane. The intensity data were collected at 173K (−100°) with a *Stoe-Mark-II* image plate diffraction system [28] equiped with a two-circle goniometer and with MoK_α graphite-monochromated radiation (λ 0.71073 Å). Image plate distance 130 mm, ω rotation scans 0–180° at φ 0°, and 0–168° at φ = 90°, step $\Delta\omega$ = 1.0°, exposures of 3 min per image, 2θ range 1.76–52.59°, $d_{min}-d_{max}$ = 23.107–0.802 Å. The structure was solved by direct methods with the programme SHELXS-97 [29]. The refinement and all further calculations were carried out with SHELXL-97 [29]. The NH H-atoms were located in a difference *Fourier* map and were freely refined. The C-bound H-atoms were included in calculated positions and treated as riding atoms: C–H = 0.95, 0.99, 0.98, and 1.00 Å for CH(arom), CH_2, Me, and CH(methine), resp., with $U_{iso}(H) = k \cdot U_{eq}$ (parent C-atom), where k = 1.5 for Me H-atoms and k = 1.2 for all other H-atoms. The non-H atoms were refined anisotropically, with weighted full-matrix least-squares on F^2. A semi-empirical absorption correction was applied with the MULscanABS routine in PLATON [30].

*Methyl 5-[1-Methyl-1-[1-(phenylmethyl)pyrrolidin-2-yl]ethyl]-1*H*-pyrrole-2-carboxylate* (**7**). According to [27a] for the trichloroacetylation of the 1*H*-pyrrole moiety [27a] and to [27b] for the ester formation: A soln. of **4** (218 mg, 0.8 mmol, 1 equiv.) in anh. THF (1.5 ml) was slowly added to a soln. of

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[4]) CCDC-907947 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif.

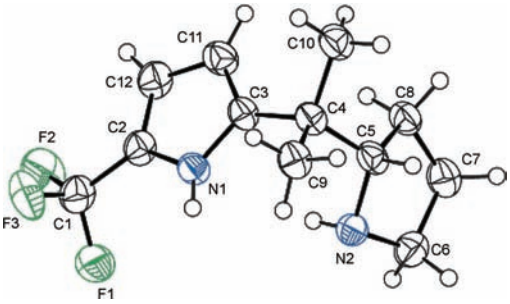

Fig. 4. *The molecular structure and crystallographic numbering scheme of the compound* **6**. Displacement ellipsoids at the 50% probability level.

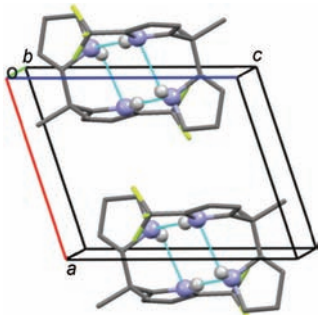

Fig. 5. *Crystal packing of compound* **6**, *viewed along the* b-*axis showing the formation of the N–H···N H-bonded square formed by two inversion-related molecules.* H-bonds are shown as dashed cyan lines; the C-bound H-atoms are omitted for clarity.

trichloroacetyl chloride (0.1 ml, 0.9 mmol, 1.1 equiv.) in anh. THF (1 ml) and the resulting yellow-brown soln. was stirred at r.t. under N_2. After 10 min, a precipitate formed, and the mixture was stirred for a total of 1.5 h at r.t.. Then the precipitate was collected by filtration, washed with cold Et_2O (4 ×) and dried under vacuum, to afford 304 mg (92%) of a white solid, which was used without further purification. The solid (265 mg, 0.64 mmol) was dissolved in anh. MeOH, MeONa (90 mg, 1.66 mmol, 2.6 equiv.) was added in two portions (initially and after 3 h), and the mixture was stirred for 5 h at r.t. under N_2. Then additional MeONa (45 mg, 0.83 mmol, 1.3 equiv.) was added, and the mixture was stirred at 40° for 18 h. The solvent was evaporated, and H_2O (20 ml) and AcOEt (20 ml) were added. The aq. phase was extracted with AcOEt (3 ×), the combined org. phase dried (Na_2SO_4), and the solvent evaporated: **7** (140 mg, 59% over 2 steps). Yellow oil, which was used for the next step without further purification. IR (KBr): 3338.9*s* (br.), 2965.2*s*, 2868.3*m*, 2806.7*w*, 1694.7*s*, 1560.8*m*, 1488.5*m*, 1314.7*m*, 1244.8*m*, 1194.4*m*, 1155.2*m*, 1104.9*m*, 1034.8*m*, 1004.3*m*, 929.3*m*, 791.3*s*, 763.0*s*, 698.9*s*. ^{1}H-NMR ($CDCl_3$): 10.75 (br. *s*, H–N(1)); 7.48–7.37 (*m*, 4 H (Ph)); 7.26–7.32 (*m*, 1 H (Ph)); 6.84–6.83 (*m*, H–C(3)); 6.02–6.01 (*m*, H–C(4)); 4.16 (*d*, *J* = 13.7, 1 H, PhCH_2); 3.82 (*s*, COOMe); 3.57 (*d*, *J* = 13.7, 1 H, PhCH_2); 2.85 (*dd*, *J* = 8.6, 5.9, H–C(2″)); 2.81 (*m*, 1 H, CH_2(5″)); 2.41 (*dt*, *J* = 10.4, 6.8, 1 H, CH_2(5″)); 1.96–1.85 (*m*, 1 H, CH_2)3″)); 1.58–1.49 (*m*, 1 H, CH_2(4″)); 1.45 (*s*, Me); 1.42–1.34 (*m*, 1 H, CH_2(3″)); 1.29 (*s*, Me); 1.18–1.08 (*m*, 1 H, CH_2(4″)). ^{13}C-NMR ($CDCl_3$): 161.5 (*C*OOMe); 144.6 (C(5)); 140.3 (C_{ipso}); 128.5 (CH(Ph)); 128.0 (CH(Ph)); 126.9 (CH(Ph)); 121.2 (C(2)); 114.7 (C(3)); 107.1 (C(4)); 74.6 (C(2″)); 63.4 (Ph*C*H_2); 54.9 (C(5″)); 51.1 (COO*Me*); 39.2 (Me_2*C*(1′)); 29.6 (Me); 29.0 (C(3″)); 24.7 (Me); 24.2 (C(4″)). ESI-MS: 363.3 (10), 349.2 (50, $[M+Na]^+$), 327.3 (100, $[M+H]^+$). HR-ESI-MS: 327.2069 ($C_{20}H_{27}N_2O_2^+$, $[M+H]^+$; calc. 327.2067).

*Methyl 5-[1-Methyl-1-(pyrrolidin-2-yl)ethyl]-1*H*-pyrrole-2-carboxylate* (**8**). To a soln. of **7** (140 mg, 0.43 mmol, 1 equiv.) in EtOH (20 ml) was added 10% Pd/C (45 mg, 0.1 equiv. Pd), and the suspension was shaken under 2 bar H_2 at r.t. overnight. The mixture was then filtered on *Celite*, the *Celite* pad thoroughly washed with CH_2Cl_2, the solvent evaporated, and the crude product purified by CC (neutral alumina gel, 0.5% MeOH/CH_2Cl_2): 72 mg (72%) of **8**. Yellow paste. IR (KBr): 3342.5*s* (br.), 2966.6*s*,

2869.4*s*, 1701.3*s*, 1559.3*m*, 1489.9*s*, 1463.7*m*, 1317.5*m*, 1231*m*, 1160.2*m*, 1103.5*m*, 1039.2*m*, 1002.9*m*, 929.4*m*, 791.7*m*, 764.9*s*. ^{1}H-NMR ($CDCl_3$): 11.1 (br. *s*, H–N(1)); 6.79 (*d*, *J* = 3.7, H–C(3)); 5.96 (*d*, *J* = 3.7, H–C(4)); 3.81 (*s*, MeO); 3.11 (*t*, *J* = 8.2, H–C(2″)); 2.91 (*t*, *J* = 6.7, CH_2(5″)); 1.83 (br. *s*, H–N(1″)); 1.80 – 1.71 (*m*, 1 H, CH_2)3″)); 1.68 – 1.50 (*m*, CH_2(4″)); 1.30 (*s*, Me); 1.23 (*s*, Me); 1.16 – 1.06 (*m*, 1 H, CH_2(3″)). ^{13}C-NMR ($CDCl_3$): 161.8 (*C*OOCH$_3$), 145.3 (C(5)); 120.9 (C(2)); 114.5 (C(3)); 106.8 (C(4)); 68.4 (C(2″)); 51.0 (MeO); 46.6 (C(5″)); 37.6 (Me$_2$*C*(1′)); 29.3 (Me); 27.1 (C(3″)); 25.9 (C(4″)); 24.5 (Me). EI-MS: 237.01 (10, $[M+H]^+$), 134.08 (15), 70.1 (100, $C_4H_8N^+$). HR-ESI-MS (pos.): 237.1596 ($C_{13}H_{20}N_2O_2^+$, $[M+H]^+$; calc. 236.1525).

Compounds **3a** *and* **3b** (racemic). To a soln. of **2** (150 mg, 0.84 mmol, 1 equiv.) in anh. toluene (0.2 ml) and molecular sieves *Fluka* 4 Å was added a soln. of (*E*)-cinnamaldehyde (127 mg, 0.96 mmol, 1.14 equiv.) in toluene (0.65 ml), and the mixture was stirred at r.t. overnight under N_2. Then the solvent was evaporated, the product dissolved in CH_2Cl_2, and the solvent evaporated (procedure repeated 5 ×), to yield a yellow solid (215 mg, 88%) as a mixture of starting materials, **3a**, **3b**, and a not completely identified by-product (ratio **3a**/**3b** 14 : 1 by ^{1}H-NMR). The crude mixture was purified by CC (neutral alumina, 1% MeOH/CH_2Cl_2; then basic alumina, CH_2Cl_2): **3a** (74 mg, 30%). Due to its low ratio in the crude mixture and to the difficulty of the purification, **3b** was characterized only by 1D and 2D ^{1}H-NMR of the crude mixture.

*(4*RS*,8a*SR*)-4,6,7,8,8a,9-Hexahydro-9,9-dimethyl-4-[(1*E*)-2-phenylethenyl]-1*H*-pyrrolo[3,2-*f*]indolizine* (**3a**): Orange solid. ^{1}H-NMR (C_6D_6): 7.29 (*d*, *J* = 7.3, 2 H_o); 7.09 (*t*, *J* = 7.45, 2 H_m); 7.03 (*t*, *J* = 7.1, H_p); 6.75 (br. *s*, H–N(1)); 6.68 (*d*, *J* = 15.8, PhC*H*=CH); 6.44 (*dd*, *J* = 15.8, 8.6, PhCH=C*H*); 6.31 (*t*, *J* = 2.6, H–C(2)); 6.13 (*t*, *J* = 2.6, H–C(3)); 3.98 (*d*, *J* = 8.6, H–C(4)); 3.32 (*t*, *J* = 8.1, CH_2(6)); 2.53 – 2.49 (*m*, 1 H, H–C(8a)); 2.26 – 2.20 (*m*, CH_2(6)); 1.75 – 1.65 (*m*, 1 H, CH_2(7)); 1.65 – 1.53 (*m*, 3 H, CH_2(8), CH_2(7)); 1.27 (*s*, Me); 0.97 (*s*, Me). ^{13}C-NMR (C_6D_6): 137.9 (C_{ipso}); 134.8 (C(9a)); 134.5 (PhCH=*C*H); 130.6 (PhCH=CH); 128.7 (2 C_m); 127.3 (C_p); 126.8 (2 C_o); 118.3 (C(3a)); 116.8 (C(2)); 105.8 (C(3)); 70.5 (C(8a)); 66.5 (C(4)); 53.7 (C(6)); 34.8 (C(9)); 25.0 (Me); 24.0 (C(8)); 23.6 (Me); 22.9 (C(7)).

*(5*RS*,10a*RS*)-2,3,10,10a-Tetrahydro-10,10-dimethyl-5-[(1*E*)-2-phenylethenyl]-1*H*,5*H*-dipyrrolo[1,2-c:2′,1′-f]pyrimidine* (**3b**): ^{1}H-NMR (C_6D_6): 7.25 (*d*, *J* = 7.5, 2 H_o); 7.03 – 7.09 (n/d, 3 H, 2 H_m, H_p); 6.61 (*dd*, *J* = 2.8, 1.7, 1 H–C(7)); 6.52 (*d*, *J* = 16, PhC*H*=CH); 6.41 (n/d, H–C(8)); 6.23 (*dd*, *J* = 16, 8.3, PhCH=C*H*); 6.2 (*dd*, *J* = 3.4, 1.7, H–C(9)); 4.42 (*d*, *J* = 8.3, H–C(5)); 2.96 (*m*, 1 H, CH_2(3)); 2.36 (*m*, H–C(10a)); 1.94 (*m*, 1 H, CH_2(3)); 1.55 (*m*, CH_2(2)); 1.54 – 1.47 (*m*, CH_2(1)); 1.29 (*s*, Me); 1.00 (*s*, Me).

Reaction Mixture **3a**/**3b**: ESI-MS: 293.3 (100, $[M+H]^+$), 224.3 (60).

Compounds **9a** *and* **9b** (racemic). To a soln. containing **6** (25 mg, 0.1 mmol, 1 equiv.) in anh. toluene (1 ml) was added (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol, 1 equiv.), and the mixture was stirred at r.t. overnight. Then the solvent was evaporated, the product dissolved in CH_2Cl_2, and the solvent evaporated (procedure repeated 5 ×), to yield a yellow solid (37 mg, 98%). The product was 95% pure, as determined by ^{1}H-NMR. The ^{1}H-NMR spectrum of the 5% by-product could not be completely determined, but presented a pattern similar to the two regioisomers **9a** and **9b**. We tentatively propose that the by-product is the diastereoisomer of **9a**. Compound **9b** was observed as an intermediate during the reaction (see *Supporting Material*[3])) and was identified by 1D and 2D ^{1}H-NMR.

*(4*RS*,8a*SR*)-4,6,7,8,8a,9-Hexahydro-9,9-dimethyl-4-[(1*E*)-2-phenylethenyl]-2-(trifluoromethyl)-1*H-*pyrrolo[3,2-f]indolizine* (**9a**): ^{1}H-NMR (C_6D_6): 7.78 (br. *s*, H–N(1)); 7.26 (*d*, *J* = 7.0, 2 H_o); 7.10 (*t*, *J* = 7.0, 2 H_n); 7.05 (*t*, *J* = 7.2, H_p); 6.57 (*d*, *J* = 15.8, PhC*H*=CH); 6.43 (*q*, *J* = 1.1, H–C(3)); 6.23 (*dd*, *J* = 15.8, 8.7, PhCH=C*H*); 3.75 (*d*, *J* = 8.7, H–C(4)); 3.21 (*t*, *J* = 8.3, 1 H, CH_2(6)); 2.34 (*t*, *J* = 8.1, H–C(8a)); 2.12 – 2.10 (*m*, 1 H, CH_2(6)); 1.69 – 1.58 (*m*, 1 H, CH_2(7)); 1.57 – 1.44 (*m*, 3 H, CH_2(8), CH_2(7)); 1.11 (*s*, Me); 0.74 (*s*, Me). ^{13}C-NMR (C_6D_6): 139.1 (C(9a)); 137.4 (C_{ipso}); 132.8 (PhCH=*C*H); 131.6 (Ph*C*H=CH); 128.8 (2 × C_m); 127.7 (C_p); 126.9 (2 × C_o); 122.4 (*q*, *J* = 266, CF_3); 119.7 (C(3a)); 119.0 (*q*, *J* = 39.2, C(2)); 108.3 (*q*, *J* = 3, C(3)); 70.1 (C(8a)); 66.7 (C(4)); 53.5 (C(6)); 34.9 (C(9)); 24.1 (Me); 23.8 (C(8)); 23.1 (Me); 22.8 (C(7)).

*(5*RS*,10a*RS*)-2,3,10,10a-Tetrahydro-10,10-dimethyl-5-[(1*E*)-2-phenylethenyl]-7-(trifluoromethyl)-1*H*,5*H*-dipyrrolo[1,2-c:2′,1′-f]pyrimidine* (**9b**): ^{1}H-NMR (C_6D_6): 7.22 (*d*, *J* = 7.5, 2 H_o); 7.07 – 7.05 (*m*, 2 H_m, H_p); 6.78 (*d*, *J* = 3.9, H–C(8)); 6.61 (*d*, *J* = 15.6, PhC*H*=CH); 6.11 (*dd*, *J* = 15.6, 8.1, PhCH=C*H*); 5.9 (*d*, *J* = 3.9, H–C(9)); 4.85 (*d*, *J* = 8.1, H–C(5)); 2.95 (*t*, *J* = 7.3, 1 H, CH_2(3)); 2.28 – 2.22 (*m*, H–C(10a)); 1.96 – 1.89 (*m*, 1 H, CH_2(3)); 1.45 – 1.40 (*m*, CH_2(1), CH_2(2)); 1.32 (*s*, Me); 1.10 (*s*, Me).

Reaction Mixture **9a**/**9b**: ESI-MS: 361.5 (100, $[M+H]^+$), 292.4 (20, $[M-CF_3+H]^+$).

Reaction of **2**, **6**, *or* **8** *in the Presence and in the Absence of CF_3COOH, Followed by NMR*. To a soln. of **2**, **6**, or **8** (0.015 mmol, 1 equiv.) in C_6D_6 (0.5 ml) was added (*E*)-cinnamaldehyde (0.2 ml of a 0.0825M stock soln. in C_6D_6, 0.0165 mmol, 1.1 equiv.), in an NMR tube, and the reaction was followed by NMR at r.t. For the reactions in the presence of CF_3COOH, 0.2 ml of a CF_3COOH stock soln. in C_6D_6 (0.075M, 0.015 mmol) were added instead of 0.2 ml of C_6D_6.

*Methyl (4*RS,*8a*SR*)-4,6,7,8,8a,9-Hexahydro-9,9-dimethyl-4-[(1*E*)-2-phenylethenyl]-1*H*-pyrrolo[3,2-*f*]indolizine-2-carboxylate* (**10a**): ^{1}H-NMR (C_6D_6): 8.98 (br. *s*, H–N(1)); 7.26–7.25 (*m*, 2 H_o); 7.13–7.10 (*m*, 2 H_m); 7.03–6.98 (*m*, H_p); 6.94 (br. *s*, H–C(3)); 6.60 (*d*, *J* = 15.8, PgC*H*=CH); 6.31 (*dd*, *J* = 15.8, 8.6, PhCH=C*H*); 3.81 (*d*, *J* = 8.6, H–C(4)); 3.52 (*s*, MeO); 3.24–3.20 (*m*, 1 H, CH_2(6)); 2.38–2.35 (*m*, H–C(8a)); 2.17–2.08 (*m*, 1 H, CH_2(6)); 1.66–1.56 (*m*, 1 H, CH_2(7)); 1.52–1.47 (*m*, 1 H, CH_2(7)); 1.53–1.44 (*m*, 2 H, CH_2(8)); 1.15 (*s*, Me); 0.81 (*s*, Me).

*Methyl (5*RS,*10a*RS*)-2,3,10,10a-Tetrahydro-10,10-dimethyl-5-[(1*E*)-2-phenylethenyl]-1*H,*5*H*-dipyrrolo[1,2-*c*:2′,1′-*f*]pyrimidine-7-carboxylate* (**10b**): ^{1}H-NMR (C_6D_6): 7.27 (*d*, *J* = 4, H–C(8)); 7.21–7.20 (*m*, 2 H_o); 7.03–7.00 (*m*, 2 H_m, H_p); 6.93 (*d*, *J* = 15.8, PhC*H*=CH); 6.20 (*dd*, *J* = 15.8, 7.09, PhCH=C*H*); 6.00 (*d*, *J* = 4, H–C(9)); 5.80 (*d*, *J* = 7.09, H–C(5)); 3.4 (*s*, MeO); 3.09–3.05 (*m*, 1 H, CH_2(3)); 2.45–2.42 (*m*, H–C(10a)); 2.18–2.10 (*m*, 1 H, CH_2(3)); 1.52–1.47 (*m*, 1 H, CH_2(2)); 1.43–1.37 (*m*, 1 H, CH_2(2)); 1.41–1.35 (*m*, 2 H, CH_2(1)); 1.36 (*s*, Me); 1.09 (*s*, Me).

*Methyl (4*RS,*8a*SR*)-4,6,7,8,8a,9-Hexahydro-9,9-dimethyl-4-[(1*E*)-2-phenylethenyl]-1*H-*pyrrolo[3,2-f]indolizine-2-carboxylate* (**10c**): ^{1}H-NMR (C_6D_6): 7.31 (*d*, *J* = 4, H–C(3)); 7.14 (*m*, 2 H_o); 7.03–6.98 (*m*, 2 H_m, H_p); 6.86 (*d*, *J* = 6.8, H–C(4)); 6.49 (*d*, *J* = 15.8, PhC*H*=CH); 6.30 (*dd*, *J* = 15.8, 6.8, PhCH=C*H*); 3.41 (*s*, MeO); 2.97–2.93 (*m*, H–C(8a)); 2.83–2.79 (*m*, 1 H, CH_2(6)); 2.52–2.50 (*m*, 1 H, CH_2(6)); 1.52–1.47 (*m*, 1 H, CH_2(7)); 1.35–1.30 (*m*, 1 H, CH_2(7)); 1.38–1.35 (*m*, CH_2(8)); 1.25 (*s*, Me); 1.19 (*s*, Me).

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